IN THE SPECIFICATION:

Please REPLACE the paragraph beginning at page 7, line 5, with the following paragraph:

Fig. 6 is a histogram showing quantitative results for the binding of I^{125}-labeled VEGF and I^{125}-labeled bFGF (basic fibroblast growth factor) to their receptors in the presence of selected three peptides (SEQ ID NO: 1, SEQ ID NO:2, and SEQ ID NO: 3) or other control peptides wherein control peptide KKKKKK has SEQ ID NO: 4.

Please REPLACE the paragraph beginning at page 7, line 9, with the following paragraph:

Fig. 7 shows curves in which radioactivity measured from ^{125}I-labeled VEGF associated with fixed peptides (Sequences 1 (SEQ ID NO: 1), 2 (SEQ ID NO: 2), and 3 (SEQ ID NO: 3)) is plotted versus molar ratios of competitors (excess free peptides) to their counterparts.

Please REPLACE the paragraph beginning at page 7, line 13, with the following paragraph:

Fig. 8 is a histogram showing radiation quantities measured from ^{125}I-labeled VEGF associated with a fixed sequence (Sequence 1 (SEQ ID NO: 1)) in the absence of and in the presence of competitors (excess non-labeled VEGF, free Sequences 1 (SEQ ID NO: 1), 2 (SEQ ID NO: 2), and 3 (SEQ ID NO: 3)).

Please REPLACE the paragraph beginning at page 7, line 18, with the following paragraph:

Fig. 9 provides histograms in which the radioactivity measured from ^{125}I-labeled VEGF associated with fixed Sequence 1 (RRKRRR) (SEQ ID NO: 1) is plotted in the absence of competitors and in the presence of competitors for various VEGF isoforms.

Please REPLACE the paragraph beginning at page 8, line 4, with the following paragraph:

Fig. 11 gives photographs of rabbit corneal domes showing the obvious angiogenesis in the test groups treated with VEGF only (A), the anti-angiogenic effect in the test group treated simultaneously with both Sequence 1 RRKRRR (SEQ ID NO: 1) and VEGF (B), and the obvious angiogenesis in the test group treated with the peptide EEFDDA (C) (SEQ ID NO: 5).

Please REPLACE the paragraph beginning at page 8, line 13, with the following paragraph:

Fig. 13 shows curves in which viability of human fibro sarcoma cell line is plotted versus concentrations of peptides, demonstrating that the peptides of the invention (SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3) have no direct influence on human fibro sarcoma cells.

Please REPLACE the paragraph beginning at page 8, line 17, with the following paragraph:

Fig. 14 shows curves in which changes in tumor size are recorded over the time period of injection, demonstrating that the peptide of Sequence 1 (SEQ ID NO: 1) effectively inhibits the growth of human colon carcinoma cells in mice.

Please REPLACE the paragraph beginning at page 8, line 21, with the following paragraph:

Fig. 15a is a histogram in which the numbers metastatic nodules from spleen to liver are measured after treatment with saline solution and with various peptides (SEQ ID NO: 1, SEQ ID NO: 4, and SEQ ID NO: 5).

Please REPLACE the paragraph beginning at page 8, line 24, with the following paragraph:

Fig. 15b is a histogram in which the weights of mouse livers to which the human colon carcinoma cells are transferred from the spleen are measured after treatment with various peptides (SEQ ID NO: 1, SEQ ID NO: 4, and SEQ ID NO: 5).

Please REPLACE the paragraph beginning at page 12, line 18, with the following paragraph:

An examination which was made for the inhibitory activity of the 12 peptides against the binding of VEGF to its receptors verified that the peptide of sequence 1 (SEQ ID NO: 1) (NH_2-Arg-Arg-Lys-Arg-Arg-Arg-$CONH_2$), the peptide of sequence 2 (SEQ ID NO: 2) (NH2-Arg-Lys-Lys-Arg-Lys-Arg-$CONH_2$), and the peptide of sequence 3 (SEQ ID NO: 3) (NH_2-Arg-Arg-Arg-Arg-Arg-Arg-$CONH_2$) are the most potent inhibitors against VEGF activity.

Please REPLACE the paragraph beginning at page 27, line 21, with the following paragraph:

Each peptide was examined for antagonistic activity against VEGF in the same manner as

in Example 2. Referring to Fig. 9, the radioactivity measured from ^{125}I-labeled VEGF associated with fixed Sequence 1 (RRKRRR) (SEQ ID NO: 1) is plotted in the absence of competitors and in the presence of competitors for various VEGF isomers. From the fact that Sequence 1 (RRKRRR) (SEQ ID NO: 1) inhibited not only the binding of labeled $VEGF_{165}$ to its receptors, but the binding of the heparin-binding domain-deficient, labeled $VEGF_{121}$ to its receptors, it can be concluded that the heparin-binding domain of VEGF is independent of the association between the peptides and VEGF. When it was taken into account that the other VEGF isoforms, $VEGF_{8-121}$, $VEGF_{109}$, and $VEGF_{8-109}$, were not inhibited from binding to their receptors by Sequence 1, the amino and the carboxyl ends of the $VEGF_{121}$ were believed to play a key role in binding the peptide to VEGF.

Please REPLACE Table 5 beginning at page 30, line 21, with the following Table:

<TABLE 5>

SAMPLE	Angiogenic activity eggs/total eggs	Angiogenic activity(%)	P[a]
WATER	3/28	10.8(1.4)[0]	
VEGF (10ng)	9/27	33.6 (3.8)	0.004
VEGF+RRKRRR (SEQ ID NO: 1) (1μg)	4/26	15.6(5.1)	0.245
VEGF+RKKRKR (SEQ ID NO: 2) (1μg)	4/26	15.6 (4.5)	0.2 71
VEGF+RRRRRR (SEQ ID NO: 3) (1μg)	4/26	15.6(5.1)	0.245
VEGF+KKKKKK (SEQ ID NO: 4) (1μg)	8/25	32.6(12.2)	0.038
VEGF+protamine (1μg)	5/26	18.8 (4.1)	0.128

Please REPLACE the paragraph beginning at page 31, line 6, with the following paragraph:

As seen in Table 5, VEGF was found to induce angiogenesis at a proportion of 33.6% in the italic model test. This angiogenic activity was effectively reduced to about 15.6% when treating egg samples with the peptides (1 μg/egg), along with VEGF and to about 18.8% when

treating egg samples with protamine (50 μg/egg), known as an antiangiogenic factor, along with VEGF. However, a control peptide (KKKKKK, SEQ ID NO: 4), which was not selected in spite of its similar properties to those of the screened peptides, did not show anti-angiogenic activity as it induced angiogenesis at a proportion of about 32.6%.

Please REPLACE the paragraph beginning at page 31, line 17, with the following paragraph:

To confirm the test results obtained from egg CAM, an experiment was performed using rabbit corneal domes for *in vivo* angiogenesis testing. New Zealand male rabbits weighing 3 kg (SLC, Japan) were subjected to intramuscular ketamine anesthesia (44 mg/kg), followed by dissecting the corneal domes to a length of 3 mm by use of an operating knife (Bard-Parker - #11) . VEGF (10 ng, R&D systems) was dropped, alone or in combination with 1 μg of a peptide of an amino acid sequence EEFDDA (SEQ ID NO: 5) or Sequence 1 (RRKRRR) (SEQ ID NO: 1), onto a Thermanox coverslip (Nunc) and dried under germ-free conditions, after which the coverslips were placed on the dissected areas which were then observed for natural healing. 6 rabbits were used per test group within which all animals were observed to show similar results. 16 days after the operation, angiogenesis was obviously observed and photographs were taken of blood vessels newly formed in the corneal dome (Nikon, FS-2, Japan). As seen in photographs of Fig. 11, the control peptide EEFDDA (SEQ ID NO: 5) had no influence on the VEGF-induced angiogenesis in the rabbit corneal dome (Fig. 11C) while the angiogenesis which was obviously observed in the test group treated with VEGF only (Fig. 11A) was completely inhibited in the test group treated simultaneously with both Sequence 1 RRKRRR (SEQ ID NO: 1) and VEGF (Fig. 11B).

(see next page)

Please REPLACE Table 6 beginning at page 33, line 10, with the following Table:

<TABLE 6>

SAMPLE	Angiogenic activity	Angiogenic activity(%)	P^3
No treatment	5/27	18.5(2.1)	
Cancer cell	18/24	76.0(8.5)	0.011
Cancer cell+RRKRRR (SEQ ID NO: 1) (0.1 μg)	8/22	36.0 (8.5)	0.160
Cancer cell+RKKRKR (SEQ ID NO: 2) (0.1μg)	10/23	43.0(9.9)	0.141
Cancer cell+RRRRRR (SEQ ID NO: 3) (0.1 μg)	10/24	41.0(7.1)	0.098
Cancer cell+KKKKKK (SEQ ID NO: 4) (O.1 μg)	14/22	59.0(1.4)	0.002

Please REPLACE the paragraph beginning at page 35, line 7, with the following paragraph:

It was reported that the acquirement of angiogenic ability is crucial to the progression of cancer and indispensable for the continuous growth of cancerous tissues (Hanahan, D. et al., Cell, 86, 353 (1996); Skobe, M., et al., Nature Med., 3, 1222 (1997). Also, the screened peptides were found to effectively inhibit angiogenesis in vivo. With this information, the following experiment was made to determine whether the screened peptides effectively inhibit the growth and metastasis of cancer cells. $5x10^6$ cells of HM7 were added, together with 0.5 μg/μl of an amino acid sequence EEFDDA (SEQ ID NO: 5) or Sequence 1 (RRKRRR) (SEQ ID NO: 1), to a serum-free DMEM and then introduced into male mice which were 4 weeks old (athymic nude mice, BALB/c/nu/nu, Charles River, Japan) by subcutaneous injection. From the next day, a solution of each peptide in PBS (0.5 μg/100 μl/day) was subcutaneously injected to the mice for 15 days. Sizes of the tumors thus formed were periodically measured while tumor volumes were calculated according to the following formula:

Tumor Size = 0.5 x $(\text{Diameter})^2$ x length

Please REPLACE the paragraph beginning at page 36, line 1, with the following paragraph:

In order to conduct an experiment concerning the metastasis of cancer cells to the liver, cancerous cells were transplanted into the spleen. In this regard, after being anesthetized with diethyl ether, 4-week-old male mice (athymic nude mice, BALB/c/nu/nu, Charles River, Japan) underwent flank incision. To the spleen, 100 μl of a mixture containing 10^6 cells of HM7 (human colon carcinoma cell line) and 0.5 μg/μl of amino acid sequence EEFDDA (SEQ ID NO. 5), KKKKKK (SEQ ID NO: 4), or Sequence 1 (RRKRRR) (SEQ ID NO: 1) was slowly injected, followed by the subcutaneous injection of each peptide for three weeks as in above. Four weeks after the injection, the liver was excised from each mouse and measured for weight and the size and number of metastatic nodules formed. Each test group was composed of 6-7 mice. In a student's t-test, a p value less than 0.05 was regarded as being statistically significant. In the test using tetrazolium dye (cell titer 96 Non-radioactive Proliferation Assay Kit, Promega), each peptide was evaluated to have no influence on the growth of the cancer cells ($5x10^3$ cells/well), so that the possibility that the toxicity of the peptide themselves might inhibit the growth and metastasis of cancer cells could be excluded.

Please REPLACE the paragraph beginning at page 36, line 22, with the following paragraph:

With reference to Fig. 14, changes in tumor size are recorded over the time period of injection. After 15 days of subcutaneous injection, the sequence EEFDDA (SEQ ID NO 5) exhibited no effects whereas the peptide RRKRRR of Sequence 1 (SEQ ID NO: 1) decreased the tumor size by about 28% compared to the control (PBS). Turning to Fig. 15, the numbers of metastatic nodules and liver weights after 14 days of injection are shown according to injected materials. No difference in metastasis of cancer cells could be found between the groups to which tumor was injected alone and together with the sequence EEFDDA (SEQ ID NO: 5). A weak inhibitory activity was observed in the group to which the sequence KKKKKK (SEQ ID NO: 4) was injected (about 80% of the control group to which only PBS was injected). In contrast, high inhibitory effects were found from the test group to which the peptide RRKRRR of Sequence 1 (SEQ ID NO: 1) was injected as the test group was only 16% and 33% of the control group in the number of metastatic nodules and the weight of the liver, respectively. Therefore, it is apparent that the screened peptides shield the signal transduction of VEGF to inhibit the growth and metastasis of malignant tumors.

Please REPLACE the paragraph beginning at page 37, line 16, with the following paragraph:

When the peptides of Sequences 1 (SEQ ID NO: 1), 2 (SEQ ID NO: 2), and 3 (SEQ ID NO: 3) are to be clinically used, parental routes are preferred. They are injected at an effective dose of 0.1-100 μg/kg and preferably at a dose of 0.5-10 μg/kg once a day for 2-3 weeks.

Please REPLACE the paragraph beginning at page 37, line 22, with the following paragraph:

The peptides of Sequences 1 (SEQ ID NO: 1), 2 (SEQ ID NO: 2), and 3 (SEQ ID NO: 3) were tested for acute toxicity through the following experiment.